Title: METHODS FOR DIAGNOSIS AND TREATMENT OF MDK1 SIGNAL TRANSDUCTION DISORDERS Inventor(s): CIOSSEK ET AL Appl. No.: 08/438,265

FIG. 1A

aagcggccggtctgcagtcggagacttgcaggcagcaaacacggtgcgaacgaa	90 180 232
10 20 30 M V V Q T R F P S W I I L C Y I W L L G F A H T G E A Q A A ATGGTTGTTCAAACTCGGTTCCCTTCGTGGATTATTTTGTGTTACATCTGGCTGCTTGCACACACGGGGGAGGCGCAGGCTGCG 40 50 60	322
K E V L L D S K A Q Q T E L E N I S S P P S G M E E I S G AAGGAAGTACTATTACTGGACTCGAAAGCACAACAAACAGAATTGGAATGGATTTCCTCTCCACCCAGTGGGTGG	412
TO 80 90 L D E N Y TI P I R T Y Q V C Q V M E P N Q N N W L R T N W : TTGGATGAGAACTACACTCCGATAAGAACAACCAGGTGTGCCAGGTCATGGAGCCCAACCAGAACAACTGGCTGCGGACTAACTGGATT 100 110 120	502
SKGNAQRIFVELKFTLRD©NSLPGVLGT©K TCTAAAAGGCAACGCACAAAGGATTTTTGTAGAATTCACCTTGAGGGATTGTAATAGTCTTCCCGGAGTCCTGGGAACTTGCAAG 130	592
ETFNLYYYETDYDTGRNIRENLYVKIDTIA GAAACGTTTAATTTGTACTATTATGAAACAGACTACGACACCCGGCAGGAATATACGAGAAAACCTTTATGTTAAAATAGACACCCATTGCT 160 170 180	682
A D E S F T Q G D L G E R K M K L N T E V R E I G P L S K E GCAGATGAAAGTTTCACACAAGGTGACCTTTGTCCAAAAAG	772
G F Y L A F Q D V G A C I A L V S V K V Y Y K K C W T I V E GGATTCTATCTTGCCTTTCAGGATGTAGGGGCTTGCATAGCATTGTTTGAG	862
220 240 N L A V F P D T V T G S E F S S L V E V R G T © V S S A E E AACTTAGCTGTCTTTCCAGATACAGTGACTGGTTCGGAATTTTCCTCCTTAGTCGAGGTCCGTGGGACATGTGTCAGCAGTGCCGAGGAA	952
250 270 E A E N S P R M H C S A E G E W L V P I G K C I C K A G Y Q GAGGCAGAAAATTCCCCCAGAATGCATTGCAGTACCAGAAGGAGAGGAGAGTGGCTAGTACCCATTGGAAAATGCATCTGCAAAGCAGGCTATCAG 280 290 300	1042
Q K G D T C E P C G R R F Y K S S Q D L Q C S R C P T H S CAAAAAGGGGACACTTGCGAACCCTGTGGCCGCAGGTTCTACAAATCTTCCTCTCAGGATCTCCAGTGTTCTCGTTGTCCAACCCACAGC	1132
FSDREGSSR©E©EDGYYRAPSDPPYVA©TR TTCTCTGACCGAGAAGGATCATCCAGGTGTGAATGTGAAGATGGGTACTACAGAGCTCCTTCTGATCCACCATACGTTGCATGCA	1222
340 350 360 PPS APQNLIFNINGTITVSLEWSPPADNGGRACCACACAGAACCTTATTTTCAATATCAATCAAACGACTGTAAGTTTGGAATGGAGTCCTCCGGCTGACAACGGGGGAAGA	1312
370 N D V T Y R I L © K R © S W E Q G E © V P © G S N I G Y M P AACGATGTCACCTACAGAATACTGTGTAAGCGGTGCAGTTGGGAACAGGGGAGAATGTGTGTG	1402
Q Q T G L E D N Y V T V M D L L A E A N Y T F E V E A V N G CAGCAGACGGGATTAGAGGATAACTATGTCACTGTCATGGACCTACTTGCCCATGCAAATTACACTTTCGAAGTTGAAGCTGTAAATGGA	1492
V S D L S R S Q R L F A A V S I T T G Q A A P S Q V S G V M GTTTCGGACTTAAGCAGATCCCAGAGGCTCTTCGCTGCTGTTAGCATCACCACCGGTCAAGCAGCTCCCTCGCAAGTGAGTG	1582
460 470 KERVLORSVOLSWOEPEEPNGVITEYEIKY AAGGAGCGAGTACTGCAGCGGAGTGTGCAGCTTTCCTGGCAGGAGCCGGAGCATCCCAATGGAGTCATCACGGAATATGAAATCAAGTAT	1672
490 500 510 Y E K D Q R E R T Y S T L K T K S T S A S I N N L K P G T V TATGAGAAAGATCAACGGGAAAGGACGTACTCAACACTCAAAACCAAGTCCACCTCCGCCTCCATTAATAATCTGAAACCGGGAACAGTG	1762
520 540 Y V F Q I R A V T A A G T G N Y S P R L D V A T L E E A S G TACGTCTTTCAGATCCGGGCGGTCACTGCTGCCGGTTATGGAAACTACAGCCCTAGGCTTGATGTTGCCACACTTGAGGAAGCTTCAGGT	1852

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EIC 1D
FIG. 1B 550 560 570 K M F E A T A V S S E Q N P V I I I A V V A V A G T I I L V AAAATGTTTGAAGCGACAGCAGTCTCCAGTGAACAGAATCCTGTCATCATAATTGCTGTAGTGGCTGTAGCAGGGACCATCATCTTGGTG 1942
580 FMVFGFIIGRRHCGYSKADQEGDEELYFHF TTCATGGTGTTCGGCTTCATCATTGGAAGAAGGCACTGTGGTTATAGCAAGGCTGACCAAGAAGGGGGATGAAGAACTCTACTTTCATTTT 2032
610 620 630 K F P G T K T Y I D P E T Y E D P N R A V H O F A K E L D A AAATTTCCAGGCACCAAAAACCTACATTGACCCTGAAACCTATGAGGACCCAAATAGAGCTGTCCATCAATTCGCCAAGGAGCTAGATGCC 2122
640 S C I K I E R V I G A G E F G E V C S G R L K L P G Q R D V TCCTGTATTAAAATTGAGCGTGTGATTGGTGCAGGAGAATTTGGAGAAGTTTGCAGTGCTCTTTGAAACTTCCGGGCCAGAGAGATGTT 2212
670 · 680 690 A V A I K T L K V G Y T E K Q R R D F L C E A S I M G Q F D GCAGTGGCCATAAAAACCCTGAAAGTTGGTTACACAGAAAAGCAAAGGAGGACTTTTTATGCGAAGCAAGC
700 710 720 H P N V V H L E G V V T R G K P V M I V I E F M E N G A L D CACCCAAATGTCGTCCATTT6GAAGGGGTTGTTACAAGAGGGAAGCCTGTCATGATTGTGATAGAGTTCATGGAGAATGGAGCCCTGGAT 2392
730 740 750 A F L R K H D G Q F T V I Q L V G M L R G I A A G M R Y L A GCATTTCTCAGGAAACACGATGGGCAGTTTACAGTCATTCAGTTGGTAGGAATGTTGAGGATGTTGCCGCTGCCATGCGATACTTGGCT 2482
760 770 780 D M G Y V H R D L Å A R N I L V N S N L V C K V S D F G L S GATATGGGATACGTTCACAGGGACCTTGCAGCGCGCAACATCCTTGTCAACAGCAATCTTGTTTGT
R V I E D D P E A V Y T T T G G K I P V R W T A P E A I Q Y CGGGTTATAGAGGATGATCCCGAAGCTGTCTACACCACGACTGTGGAAAAATTCCAGTAAGGTGGACTGCACCGGAAGCCATTCAATAC 2662
R K F T S A S D V W S Y G I V M W E V M S Y G E R P Y W D M CGGAAGTTCACCTCAGCCAGCGATGTGGGAGCTATGGGGATTGTCATGTGGGAAGTGATGTCTTATGGAGAAAGACCTTACTGGGACATG 2752
S N Q D V I K A I E E G Y R L P A P N D C P A G L H Q L M L TCAAATCAAGATGTCATTAAAGCGATAGAAGAAGGTTATCGTTTGCCGGCGCCCATGGATTGCCCAGCTGGTCTTCACCAGCTAATGCTG 2842
D C W Q K D R A E R P K P E Q I Y G I L D K M I R N R S S L GATTGTTGGCAGAAGATCGGGCGAAAGGCCAAAGTTTGAGCAGATAGTCGGAATTCTAGACAAAATGATTCGAAACCCAAGTAGTCTG 2932
910 930 K T P L G T C S R P L S P L L D O S T P D F T A F C S Y G E AAAACACCCCTGGGAACTTGTAGTAGACCCTTAAGCCCTCTTCTGGACCAGAGCACTCCTGACTTCACTGCCTTCTGTTCAGTTGGAGAA 3022 940 950 960
W L Q A I K M E R Y K D N F T A A G Y N S L E S V A R M T I TGGTTGCAAGCTATTAAAATGGAAAGGTATAAGGACAACTTCACAGCAGCAGCGGTTACAACTCACTC
D D V M S L G I T L V G E Q K K I M S S I Q T M R A Q M L H GATGATGTGATGAGTTTAGGGGATCACACTGGTTGGCCATCAAAAGAAGATCATGAGCAGCATCCAGACTATGCGGGCACAAATGTTGCAT 3202
L H G T G I Q V * TTACACGGAACAGGCATCCAAGTGTGA 3229
cacatcggcctccctcagatgaggcttaagactgcaggagaacagttctggccttcagtatacgcatagaatgctgctagaagacagttg 3319 atatactgggtccttcctacaagaaagagaagatttagaagcacctccagacttgaactcctaagtgccaccagaatatacaaaaaggg 3409 aatttaggatccaccactggtggccaggaacacagcagagacaataaaacaaagtactacctgaaaaacatcccaacaccttgagctctcg 3499 aacctcctttttatcttatagactttttaaaaaatgtacataaagaatttaagaaaga
gttaaaatcaatgaaatattttccttaaaatatgtgatttcagactattcttttccagaaccatctgtgtttattctgcttaaggacttt 3679 gttttagaaagttatttgtagctttggacctttttagtgttaaatttatgacacgttactacactgggaacctttgaagactctcaaact 3769 taaaggaaagcaaaactacgcacatagtcgaggatggactttgtccttcatggctttggtatcctggctgtgtcatttgttaaaccagt 3859 gatgttttcatattgtttgctgattggcaggtagttcaaaattgcaagttgccaagagctctgatattttttaacaggatttttttt

IG. 2A

MDK1'-T1

2002	2182 2272 2362 2452 2542 2632 2722 2812 2901
590 C G Y S K A D Q STGTGGTTATAGCAAGGCTGACCAA cgcaacaataactgtttaagacaat	tacattctgcttattttgttgttat taaatataaagacattgttctga gatatagtgtaattttcttcattgc tattgtaattgaatttgatataaag tgatactatgttgtttcaattttga gaaaagtttatataaaccatttctc cactttgtatatccagcctctatta tcatatcttgtactaattttatgta aaaaaaaaaa
570 580 580 590 V A V A G T I I L V F M V F G F I I G R R H C G Y S K A D Q GTGGCTGTAGCAGGGACCATCATCTTGGTGTTCATGGTTCATCATTGGAAGGCACTGTGGTTATAGCAAGGCTGACCAA 600 610 E G D ·E E L Y F H S L V T N E H L S V L * GAAGGGATGAAGAACTCTACTTTCATTCTTTAGTAACAAATGAGCACCTGTCAGTTTTAAGCAAGGCTGACCAA	caattttggataaacaatcaactacagcagaataaatcaagatttttaagtcccattttcctttatacattctgcttattttgttgttat atgtttattttttaaaccatcgatcttgattgaatgtgataccataagcacagttaggctgcagtgtaaatatataaaagacattgttctgagagcagtatttttttaaggatatagggcattgtttgt
570 V A V A G T I I L V F M V F G F I I G R GTGGCTGTAGCAGGACCATCATCTTGGTGTTCATGGTGTTCGGCTTCATCATTGGAAGA 600 E G D ·E E L Y F H S L V T N E H L S V L GAAGGGATGAAGAACTCTACTTTCATTCTTTAGTAACAAATGAGCACCTGTCAGTTTTA	caattttggataaacaatcaactacagcag atgtttattttttaaactctgatcttgati gagcagtacgatttcatggaaagattgtti attaataaaccaaatatgcctacctatci ttgactgagcattatgtgttacctgcati ctaccttttgtgaggcatactggctacct tttcaaatcactgtcatacttggtcacgg ccctcaaggtgaatataaaactatgtctt

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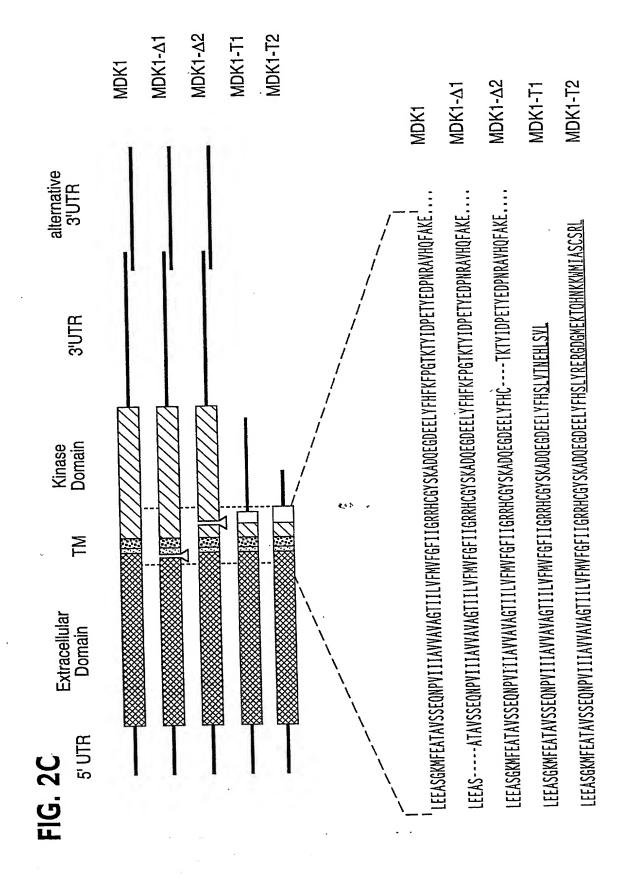
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FIG. 21

MDK1-T2

attagcattgtgaacctgactgtaatcctcttccggaaagagatgagatgctattgcgatgagaatgtacaacttgcaccttgaaatc 2272 2323 tttttgataattagtgctcaggggaggggggggggagtagaggaagcaaa Title: METHODS FOR DIAGNOSIS AND TREATMENT OF MDK1 SIGNAL TRANSDUCTION DISORDERS Inventor(s): CIOSSEK ET AL Appl. No.: 08/438,265



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